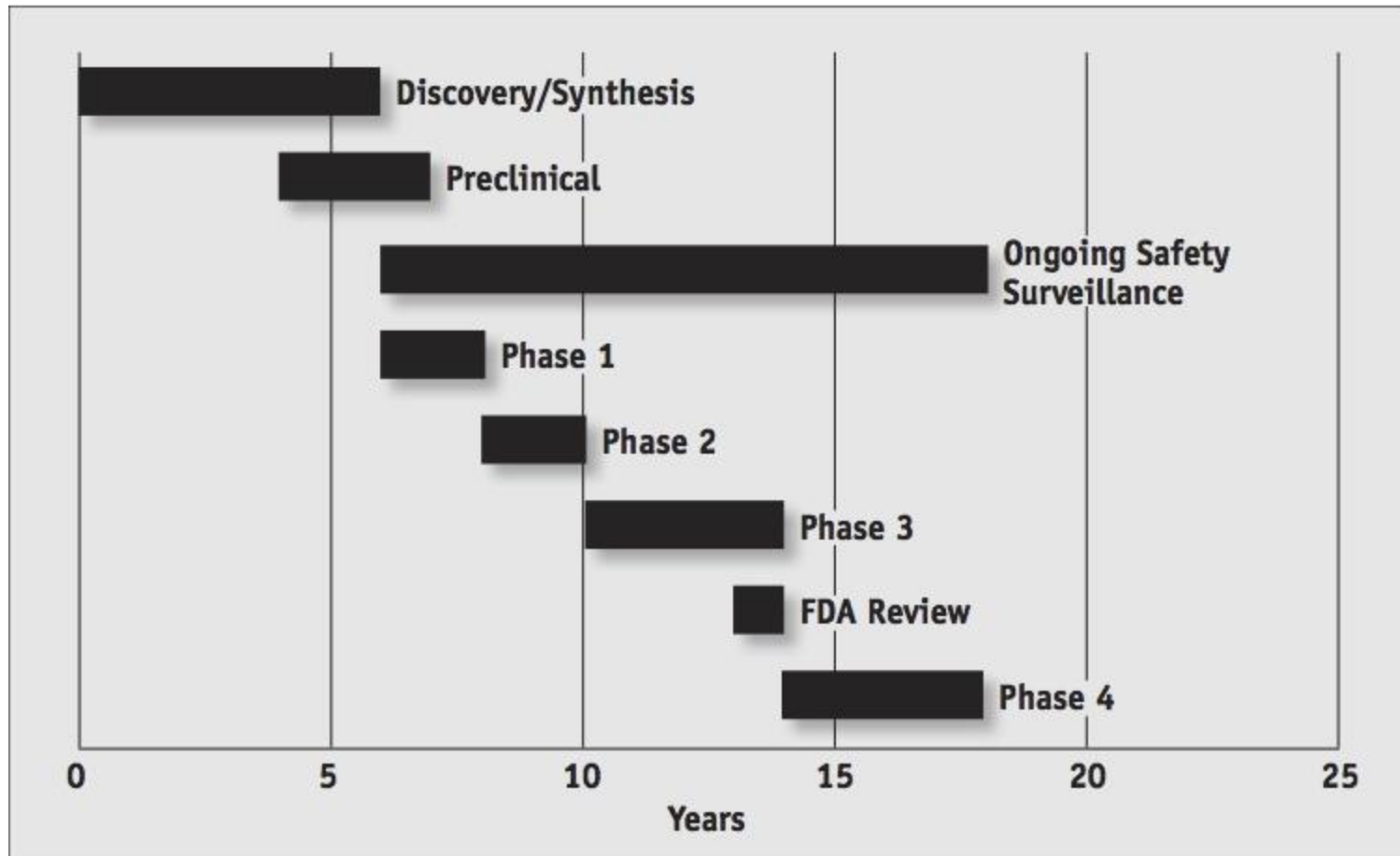


Transparency and access to medical research

Dr. Wim Weber
European editor, BMJ

Present medical research
has a credibility problem

Development timeframe of a medical intervention



What happened to:

Monoclonal antibody therapy

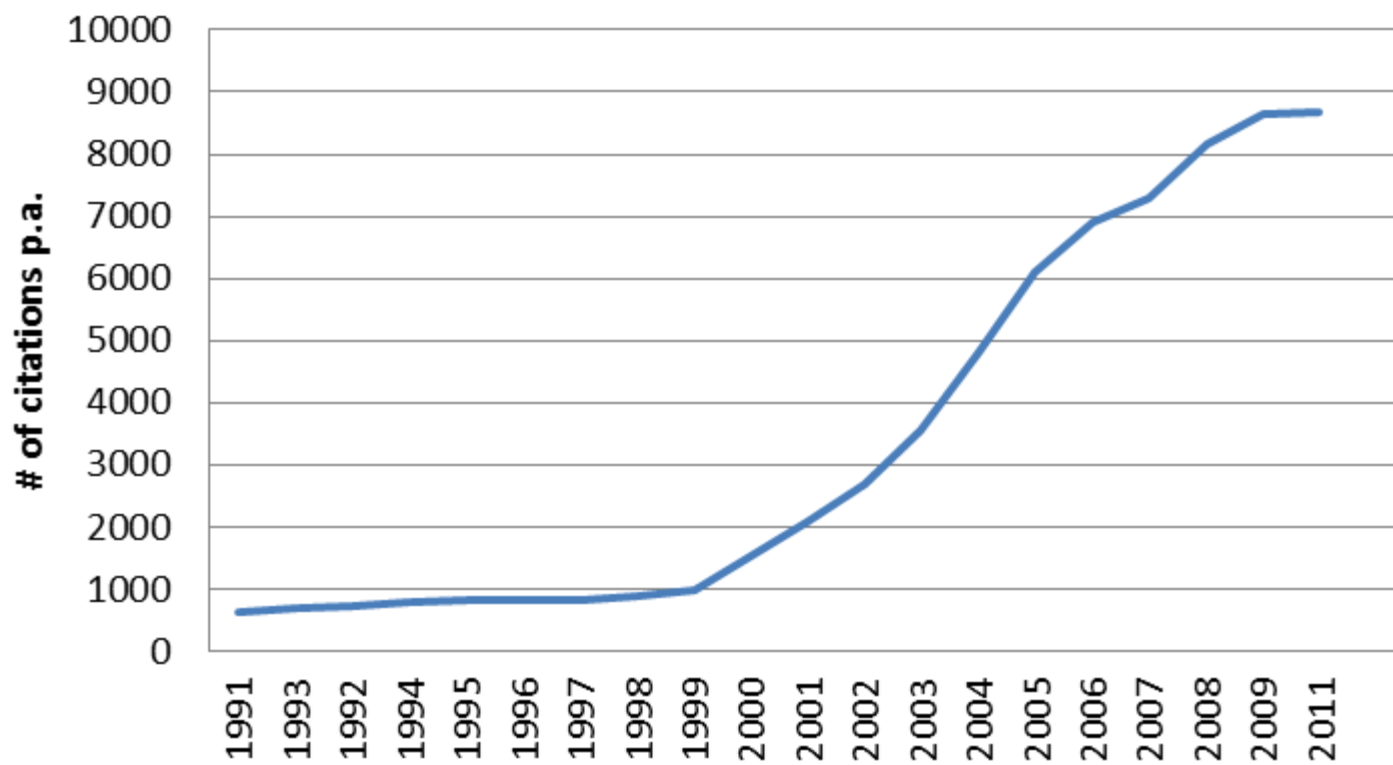
Gene therapy

Stem cell therapy

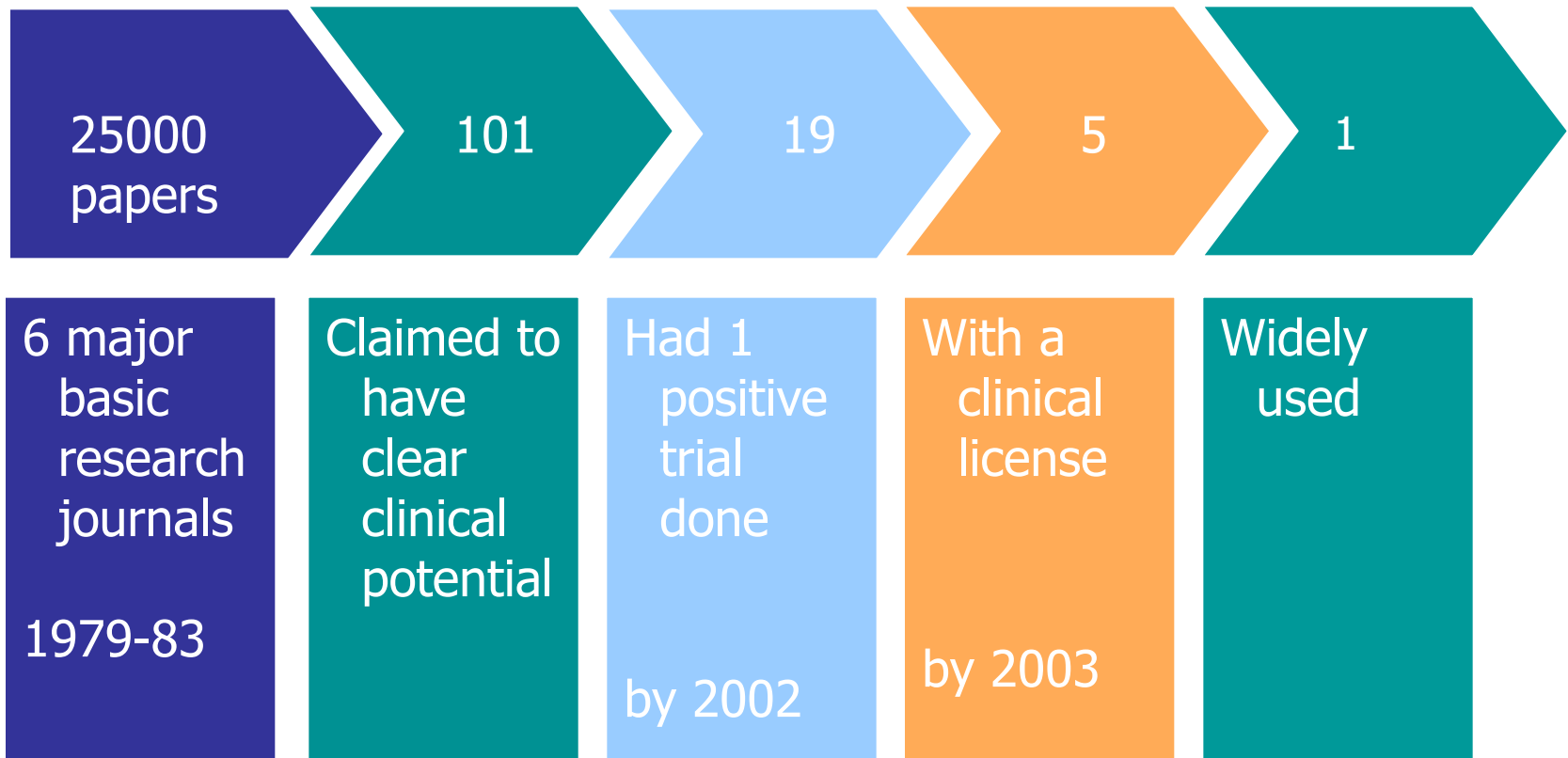
Personalised medicine

Proteomics

of 'Genomics' citations in PubMed (1991-2011)



Translation of medical research



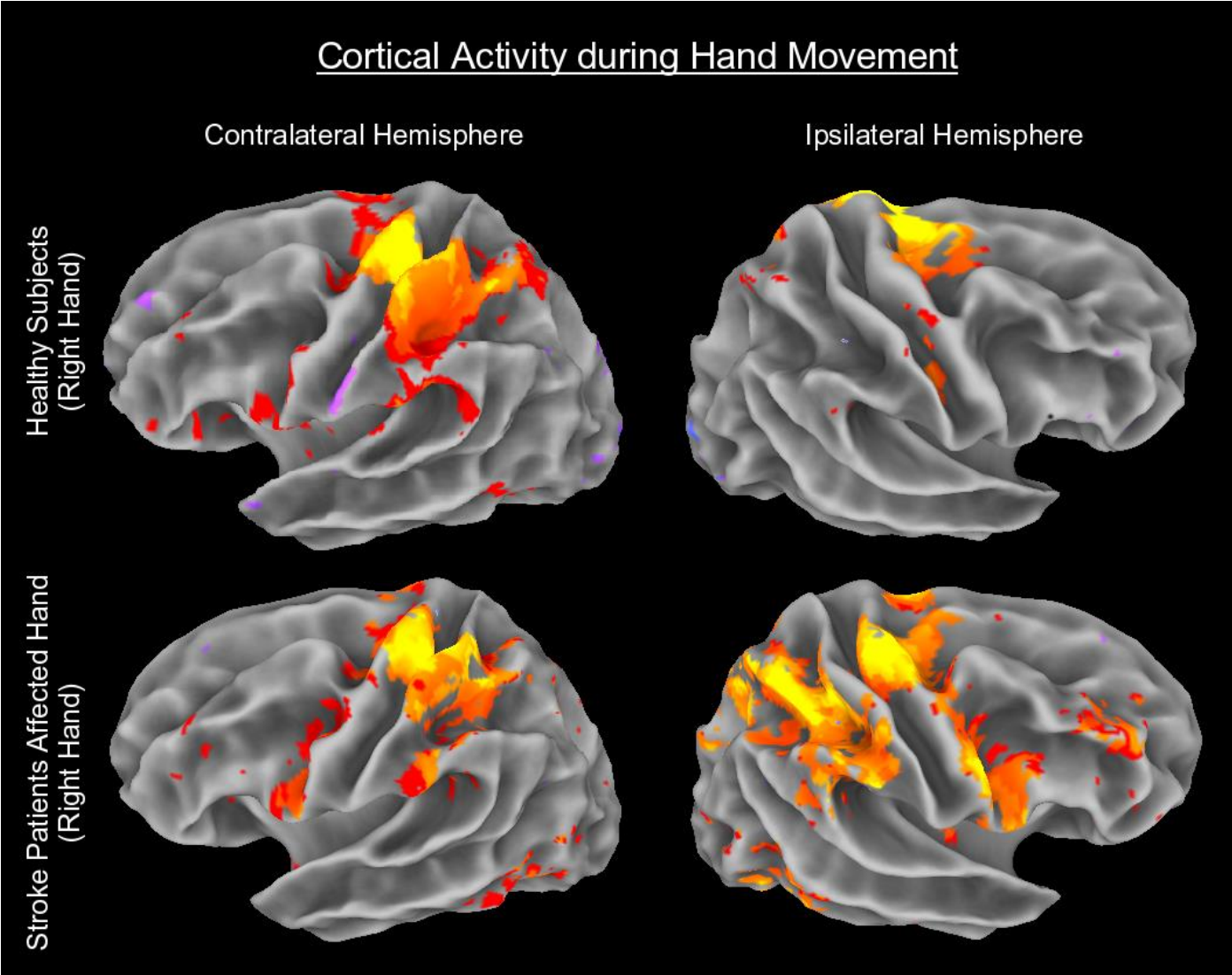
Am. J. Med. 114, 477 (2003).

What is the problem ?

Examples in basic science

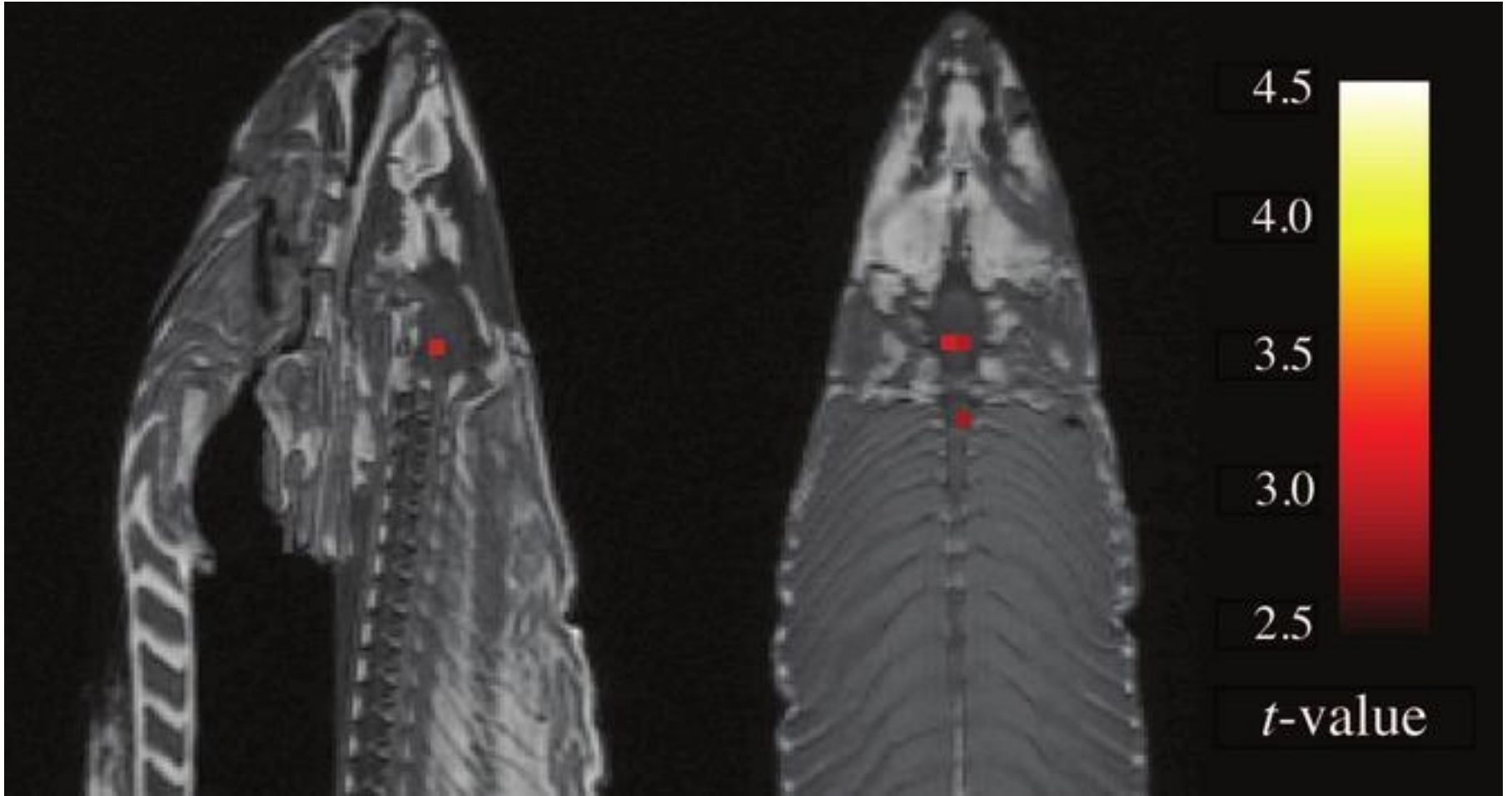


Functional MRI in neuroscience



What happens when you scan a dead fish ?

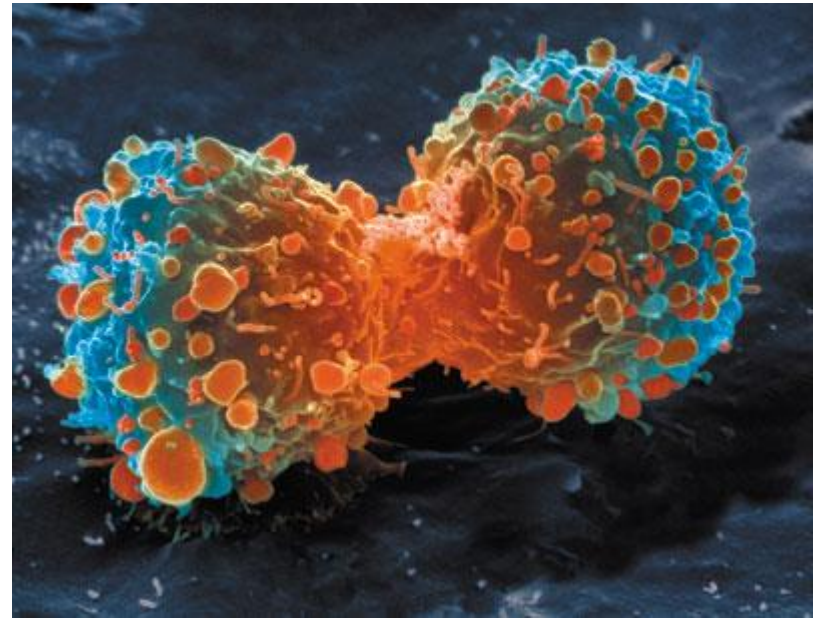




Most studies are not reproducible

Amgen researchers were
able to replicate

only 6 of 53 landmark
cancer studies



Nature 2012 Mar 28;483:531-3.

What causes this bias ?



In 4455 animal studies

3x positive studies

Overestimates of effect size

What causes this bias ?

Survey among basic researchers:

They said they publish 90% of experiments

But thought that less than 50% of other animal experiments are published.

Employees of for-profit organizations estimated that 10% are published.

OPEN ACCESS

ESSAY

968,189

VIEWS

1,187

CITATIONS

6,926

SAVES

8,060

SHARES

Why Most Published Research Findings Are False

John P. A. Ioannidis

Published: August 30, 2005 • DOI: 10.1371/journal.pmed.0020124

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for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias

Claimed Research Findings May Often Be Simply Accurate Measures of the Prevailing Bias

How Can We Improve the Situation?

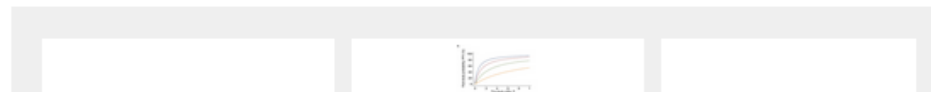
References

Reader Comments (32)

Media Coverage (38)

scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research.

Figures



Subject Areas

Clinical research de...

Gene prediction

Genetic epidemiology

Genetics of disease

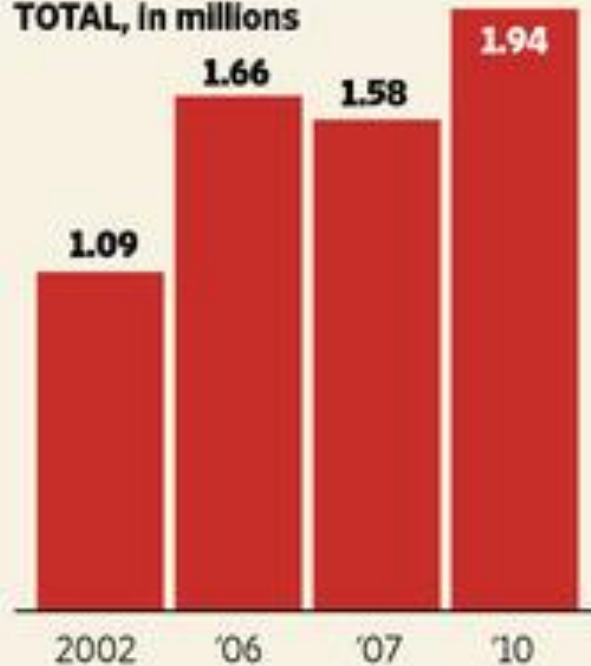
Randomized controll...



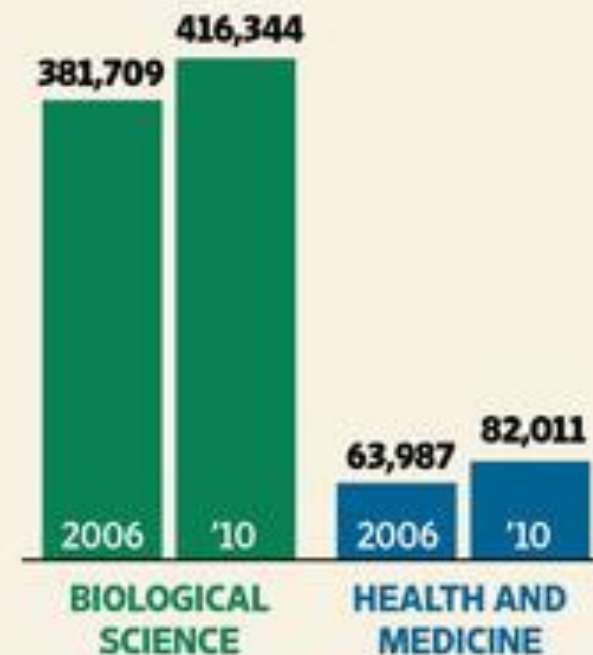
Studying Up

The number of journal articles published world-wide

TOTAL, in millions

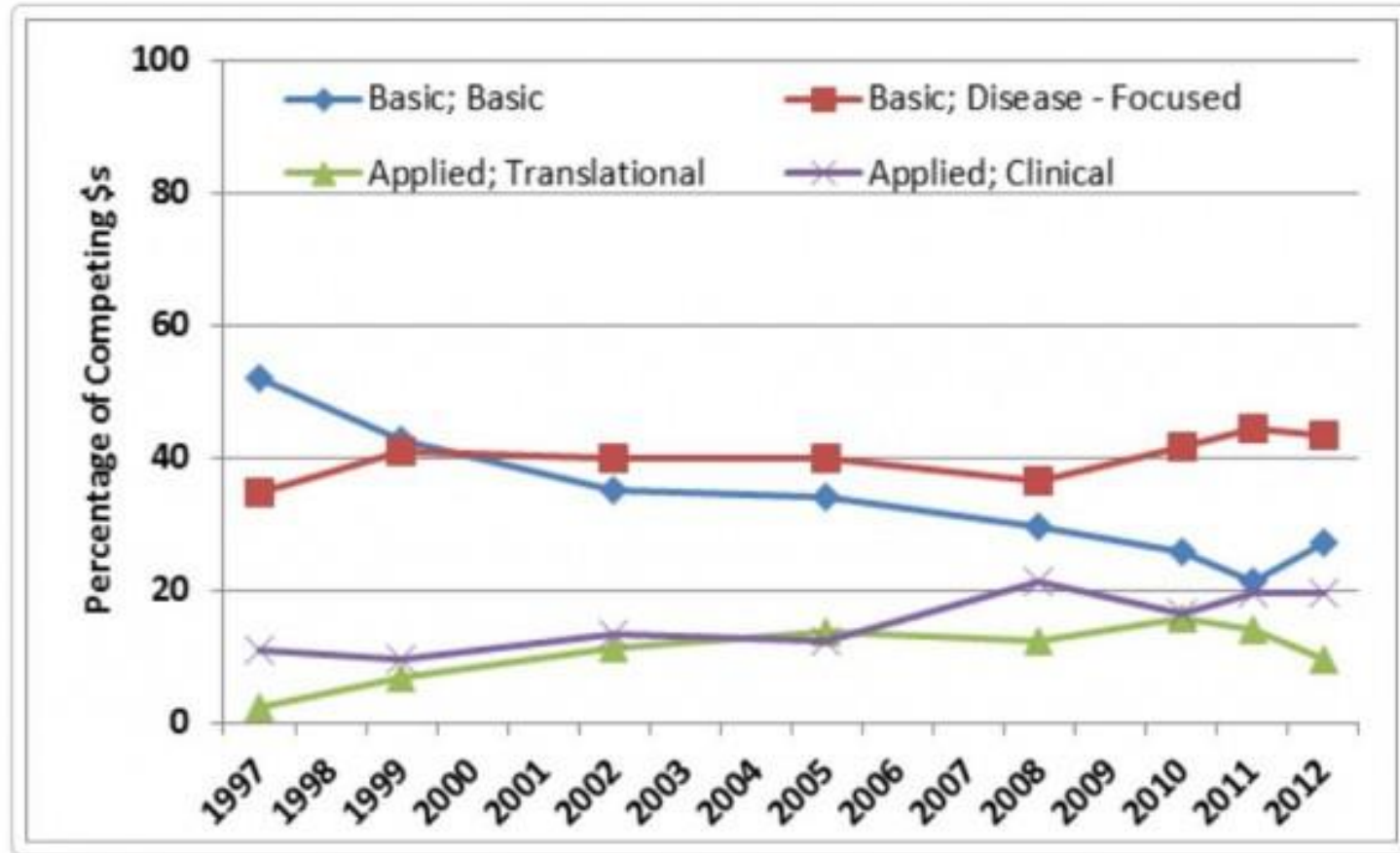


BY SUBJECT



Sources: U.K. Department for Business, Innovation and Skills; Elsevier

Money allocated to basic research



Is clinical research less biased ?

THE WALL STREET JOURNAL
Digital Network
Saturday, October 30, 2010

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EARNINGS | OCTOBER 30, 2010

Merck Books \$950 Million Vioxx Charge

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By PETER LOFTUS

Merck & Co.'s profit plunged 90% as the drug maker set aside \$950 million to pay for an anticipated resolution of a government probe of its former pain drug Vioxx.

The company's earnings excluding the Vioxx charge and other items exceeded expectations, though revenue fell short. Many drug makers have reported weak third-quarter revenue due to European pricing pressure and other challenges, but are able to offset the sluggishness with layoffs and other cost cuts.

Merck also raised the lower end of its 2010 forecast range of earnings excluding

HEALTH INDUSTRY | SEPTEMBER 24, 2010

Regulators Scuttle Drug for Diabetes

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WASHINGTON—U.S. regulators put tight curbs on the diabetes drug Avandia and European authorities said they were stopping its sales, effectively ending widespread use of a medicine that was once a multibillion-dollar-a-year seller.



View Full Image | Bloomberg News

Avandia

The Food and Drug Administration and European regulators said they were taking action on Avandia, made by GlaxoSmithKline PLC, because of data tying it to increased risk of heart attacks.

The FDA move marks a tougher stance by the agency's leadership, named last year by President Barack Obama, and signals to pharmaceutical makers and patients that mass-market drugs with troublesome side effects are getting closer scrutiny.

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Evidence in Vioxx Suits Shows Intervention by Merck Officials

By ALEX BERENSON
Published: April 24, 2005

In 2000, amid rising concerns that its painkiller Vioxx posed heart risks, Merck overruled one of its own scientists after he suggested that a patient in a clinical trial had probably died of a heart attack.

In an e-mail exchange about Vioxx, the company's most important new drug at the time, a senior Merck scientist repeatedly urged the researcher to change his views about the death "so that we don't raise concerns." In later reports to the Food and Drug Administration and in a paper published in 2003, Merck listed the cause of death as "unknown" for the patient, a 73-year-old woman.



BMJ

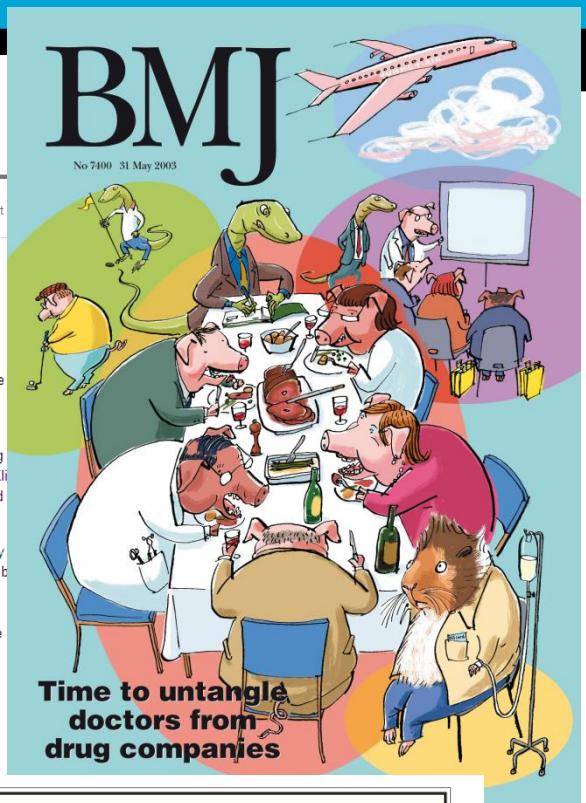
SHOULD THE DRUG INDUSTRY USE KEY OPINION LEADERS?

PLUS Does vitamin A improve child survival?
The NHS at 60: does central funding still make sense?
Endovascular stenting for caval obstruction

JOB, COURSES, CAREERS

BMJ

No 7100 31 May 2003



Time to untangle doctors from drug companies

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 | JUNE 14, 2007 | VOL. 356 NO. 24

Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes

Steven E. Nissen, M.D., and Kathy Wolski, M.P.H.

ABSTRACT

BACKGROUND
Rosiglitazone is widely used to treat patients with type 2 diabetes mellitus, but its effect on cardiovascular morbidity and mortality has not been determined.

METHODS
We conducted searches of the published literature, the Web site of the Food and Drug Administration, and a clinical-trials registry maintained by the drug manufacturer (GlaxoSmithKline). Criteria for inclusion in our meta-analysis included a study duration of more than 24 weeks, the use of a randomized control group not receiving rosiglitazone, and the availability of outcome data for myocardial infarction and death from cardiovascular causes. Of 116 potentially relevant studies, 42 trials met the inclusion criteria. We tabulated all occurrences of myocardial infarction and death from cardiovascular causes.

From the Cleveland Clinic, Cleveland. Address reprint requests to Dr. Nissen at the Department of Cardiovascular Medicine, Cleveland Clinic, 9500 Euclid Ave., Cleveland, OH 44195, or at nissen@ccf.org.
N Engl J Med 2007;356:2457-71.
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Some of the problems

- Trials measure outcomes not relevant to patients
- Failure to acknowledge earlier research
- **Non-publication of negative results**

Non-publication

Bad Pharma™

Ben Goldacre

Bestselling author of *Bad Science*

How drug companies
mislead doctors and
harm patients

364 pages





Cochrane review 2006:

Oseltamivir 150 mg daily prevented lower respiratory tract complications

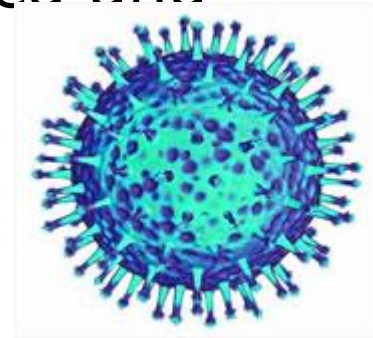
2009: Cochrane review updated, but:

- Only 2 / 10 RCTs published
- The pooled analysis was done by Roche
- Obtaining the original data has been very difficult



After 5 years Roche made all data available: and the new meta-analysis is published this week:

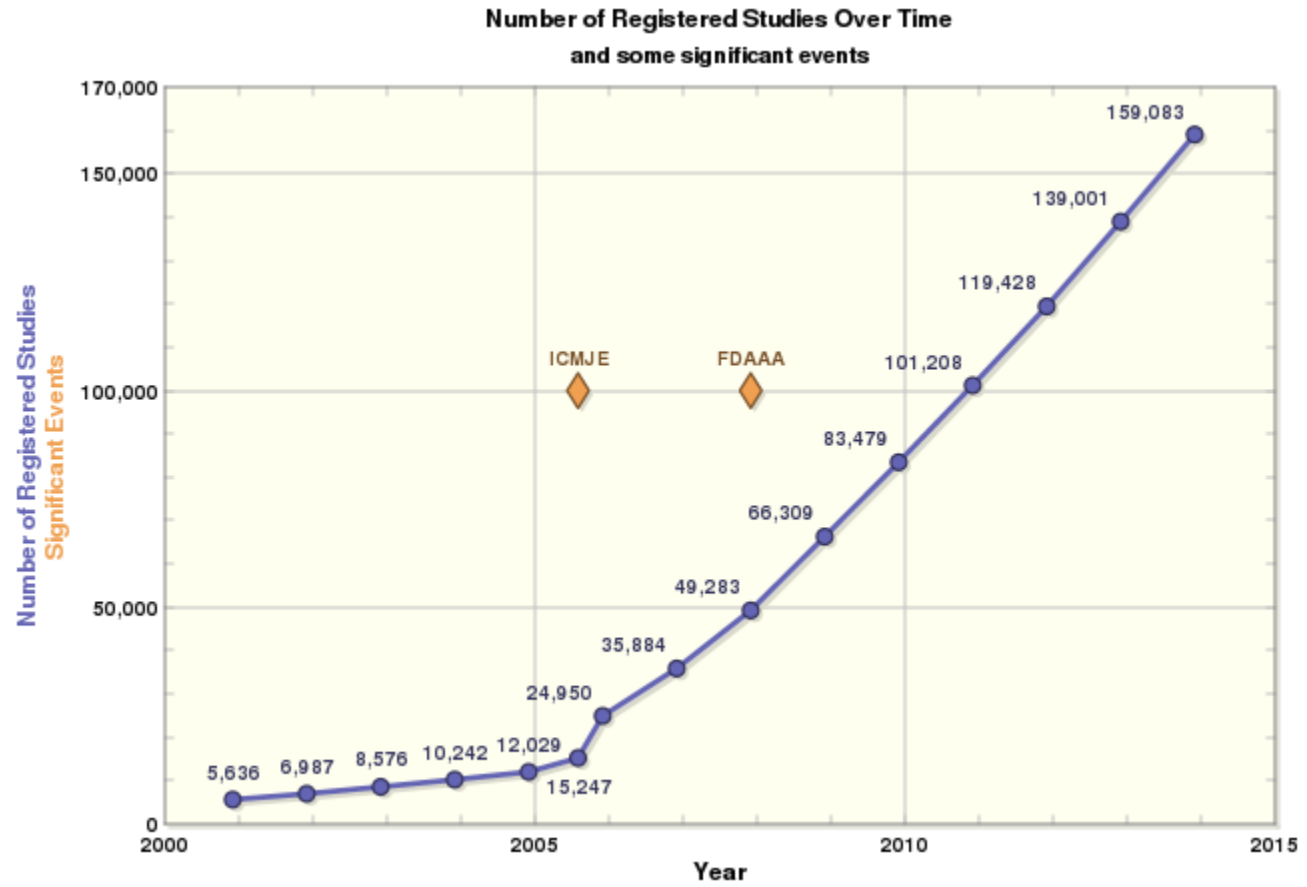
- There were **83** RCTs
- There is no evidence for effect on complications
- There are substantial side effects: nausea and psychiatric symptoms



New EU legislation

Trials must be registered

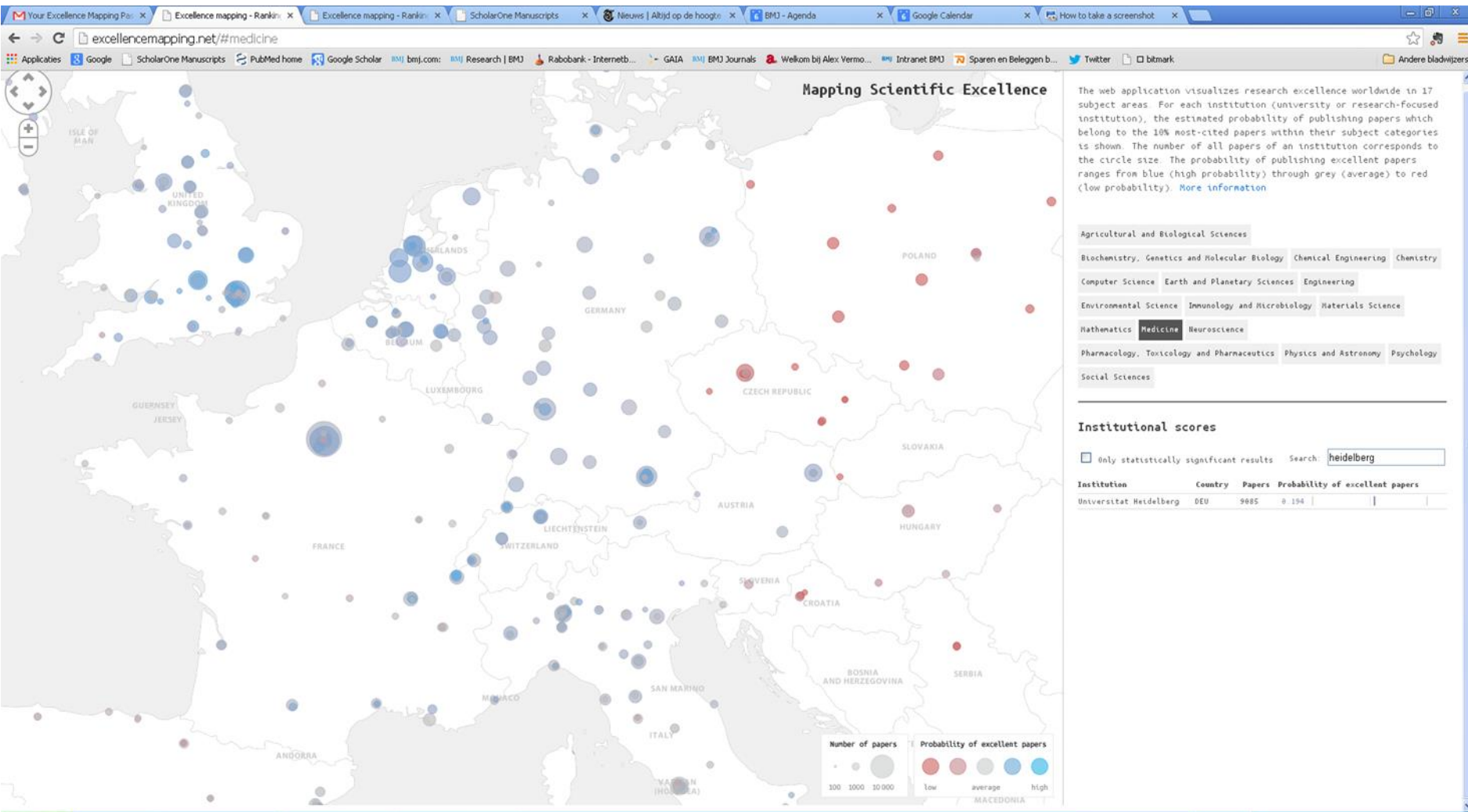
Results must be published



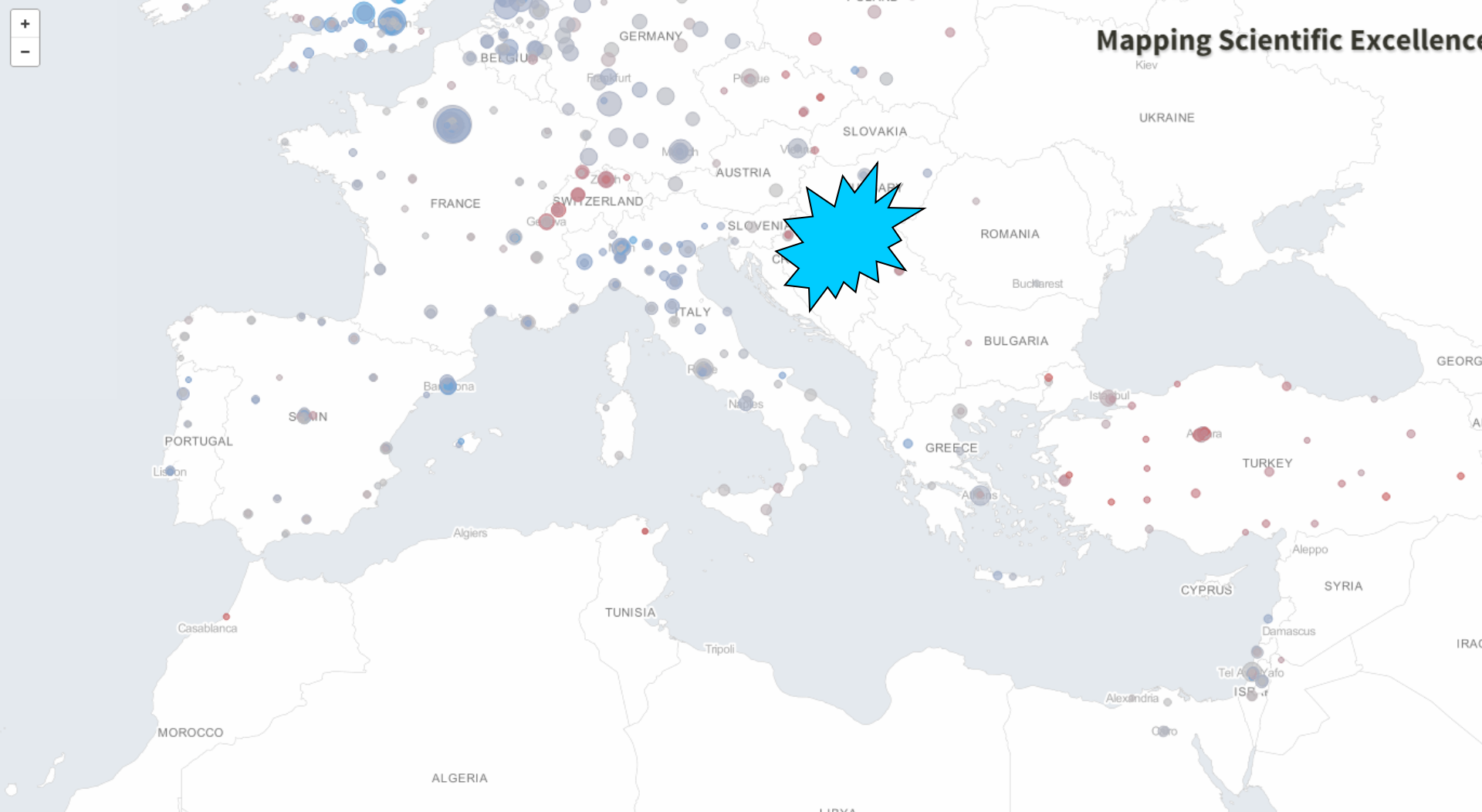
We need less basic research, but more epidemiologic research:

- Observational work validating patient-relevant outcomes
- RCTs
- Meta-analyses

Scientific excellence in Europe



Scientific excellence in Europe in 2034



Thanks

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